Improving the efficacy and tolerability of clinically validated remyelination-inducing molecules using developable combinations of approved drugs

Grant Award Details

Improving the efficacy and tolerability of clinically validated remyelination-inducing molecules using developable combinations of approved drugs

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-13063

Investigator:

Name:	Luke Lairson
Institution:	Scripps Research Institute
Type:	PI

Disease Focus: Multiple Sclerosis, Neurological Disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,554,126

Status: Pre-Active

Grant Application Details

Application Title: Improving the efficacy and tolerability of clinically validated remyelination-inducing molecules using developable combinations of approved drugs

Public Abstract:

Research Objective

The candidate is a fixed dose binary small molecule drug combination, consisting of two agents that act synergistically on a multipotent stem cell population in the CNS to stimulate remyelination.

Impact

The proposed studies will address bottleneck issues related to the effect size and tolerability of clinically validated remyelination drug classes.

Major Proposed Activities

- Establish the maximal and minimal effective concentrations (ECmin and ECmax) and associated levels of efficacy for defined combination-based drug therapies in three populations of rat OPCs.
- Establish maximal and minimal effective concentrations and associated levels of efficacy for defined drug combinations in a population of human OPCs.
- Demonstrate reproducible disease modifying activity (i.e., enhancement of remyelination efficiency) in vivo using the cuprizone model of demyelination/remyelination.
- Complete mouse brain pharmacokinetic (PK), drug-drug interaction and preliminary rodent tolerability studies for 3 OPC differentiation-inducing drug combinations.
- Complete mechanism of action studies
- Complete penultimate in vivo efficacy study with kinetic measures and imaging outputs using the cuprizone model of demyelination/remyelination.

Statement of Benefit to California:

It is estimated that >120,000 California residents suffer from multiple sclerosis (MS). This proposed research aims to provide a disease modifying therapy for MS. It will have a significant beneficial impact, by targeting the regenerative process known as remyelination, which becomes limiting during the progressive phases of MS disease.
